10/528,631

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=> d his

     (FILE 'HOME' ENTERED AT 12:23:13 ON 19 JAN 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:23:44 ON 19 JAN 2007
L1         14613 S MYOSIN (3W) KINASE?
L2          4033 S "MLCK"
L3         14977 S L1 OR L2
L4       8131756 S CLON? OR EXPRESS? OR RECOMBINANT
L5          3086 S L3 AND L4
L6        134078 S LIGHT (W)CHAIN
L7          2626 S L5 AND L6
L8          4169 S APHIS (W) GOSSYPII
L9             1 S L7 AND L8
L10         1431 S L7 AND MUSCLE?
L11          651 S CONTRACT? AND L10
L12          463 S PHOSPHORYLAT? AND L11
L13           47 S L12 AND (CARDIAC OR HEART)
L14           26 DUP REM L13 (21 DUPLICATES REMOVED)
                 E CHEN R/AU
L15         4492 S E3
                 E RUIHUA C/AU
                 E HALLING B P/AU
L16           60 S E3-E6
                 E YUHAS D/AU
L17           16 S E6-E9
                 E ALLENZA P/AU
L18           19 S E4
                 E CHAGUTURU M K/AU
L19           24 S E3-E7
L20         4599 S L15 OR L16 OR L17 OR L18 OR L19
L21            2 S L7 AND L20
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	L #	Hits	Search Text
1	L1	1	"20040241651".pn.
2	L2	87475	myosin (2w)kinase$2
3	L3	267	"MLCK"
4	L4	87481	l2 or l3
5	L5	928048	clon$3 or express$3 or recombinant
6	L6	48749	l4 same l5
7	L7	22839	light adj chain
8	L8	12663	l6 and l7
9	L9	271663	cardiac or heart or muscle$2
10	L10	9536	l8 and l9
11	L11	1623	aphis adj gossypii
12	L12	5	l10 and l11
13	L13	3088	aphis
14	L14	1623	l11 and l13
15	L15	11	contract$3 and l14
16	L16	176198	CHEN HALLING YUHAS ALLENZA CHAGUTURU
17	L17	19212	l4 and l16
18	L18	116	l14 and l16

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LOGINID:ssspta1652mxm

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

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NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 9	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 10	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 11	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 12	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 13	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 14	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 15	DEC 18	CA/CAplus patent kind codes updated
NEWS 16	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 17	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 18	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 19	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 20	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 21	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 22	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 12:23:13 ON 19 JAN 2007

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 12:23:44 ON 19 JAN 2007

FILE 'EMBASE' ENTERED AT 12:23:44 ON 19 JAN 2007
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FILE 'SCISEARCH' ENTERED AT 12:23:44 ON 19 JAN 2007
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FILE 'HCAPLUS' ENTERED AT 12:23:44 ON 19 JAN 2007
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FILE 'NTIS' ENTERED AT 12:23:44 ON 19 JAN 2007
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FILE 'LIFESCI' ENTERED AT 12:23:44 ON 19 JAN 2007
COPYRIGHT (C) 2007 Cambridge Scientific Abstracts (CSA)


=> s myosin (3w) kinase?
L1        14613 MYOSIN (3W) KINASE?

=> s "MLCK"
L2         4033 "MLCK"

=> s l1 or l2
L3        14977 L1 OR L2

=> s clon? or express? or recombinant
L4      8131756 CLON? OR EXPRESS? OR RECOMBINANT

=> s l3 and l4
L5         3086 L3 AND L4

=> s light (w)chain
L6       134078 LIGHT (W) CHAIN

=> s l5 and l6
L7         2626 L5 AND L6

=> d his

     (FILE 'HOME' ENTERED AT 12:23:13 ON 19 JAN 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:23:44 ON 19 JAN 2007
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L1         14613 S MYOSIN (3W) KINASE?
L2          4033 S "MLCK"
L3         14977 S L1 OR L2
L4       8131756 S CLON? OR EXPRESS? OR RECOMBINANT
L5          3086 S L3 AND L4
L6        134078 S LIGHT (W)CHAIN
L7          2626 S L5 AND L6

=> s aphis (w) gossypii
L8         4169 APHIS (W) GOSSYPII

=> s l7 and l8
L9            1 L7 AND L8

=> d ibib ab

L9   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2004:292143  HCAPLUS
DOCUMENT NUMBER:          140:317126
TITLE:                    Cloning and sequence of hemipteran
                          myosin light chain
                          kinase and potential use in development of
                          pesticides or pharmaceuticals
INVENTOR(S):              Chen, Ruihua; Chaguturu, Munirathnam K.; Yuhas, Debra;
                          Allenza, Paul; Halling, Blaik P.
PATENT ASSIGNEE(S):       FMC Corporation, USA
SOURCE:                   PCT Int. Appl., 21 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    ---------------------    --------
     WO 2004029577         A2    20040408    WO 2003-US29901          20030918
     WO 2004029577         A3    20040701
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2003275144         A1    20040419    AU 2003-275144           20030918
     EP 1543116            A2    20050622    EP 2003-759412           20030918
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     JP 2006500067         T     20060105    JP 2004-540171           20030918
     US 2006148031         A1    20060706    US 2005-528631           20051116
PRIORITY APPLN. INFO.:                       US 2002-413720P      P   20020926
                                             WO 2003-US29901      W   20030918
AB   The cDNA sequence and the encoded amino acid sequence of myosin
     light chain kinase from Aphis
     gossypii are disclosed.  The sequences of the invention are useful
     in the identification or development of pesticides or pharmaceuticals.


=> d his

     (FILE 'HOME' ENTERED AT 12:23:13 ON 19 JAN 2007)
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     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:23:44 ON 19 JAN 2007
L1         14613 S MYOSIN (3W) KINASE?
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L3         14977 S L1 OR L2
L4       8131756 S CLON? OR EXPRESS? OR RECOMBINANT
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L6        134078 S LIGHT (W)CHAIN
L7          2626 S L5 AND L6
L8          4169 S APHIS (W) GOSSYPII
L9             1 S L7 AND L8

=> s l7 and muscle?
L10        1431 L7 AND MUSCLE?

=> s contract? and l10
L11         651 CONTRACT? AND L10

=> s phosphorylat? and l11
L12         463 PHOSPHORYLAT? AND L11

=> s l12 and (cardiac or heart)
L13          47 L12 AND (CARDIAC OR HEART)

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14           26 DUP REM L13 (21 DUPLICATES REMOVED)

=> d 1-26 ibib ab

L14  ANSWER 1 OF 26  EMBASE  COPYRIGHT (c) 2007 Elsevier B.V. All rights
     reserved on STN                                    DUPLICATE 1
ACCESSION NUMBER:   2006526507  EMBASE
TITLE:              PKC-βII sensitizes  cardiac myofilaments to
                    Ca(2+) by phosphorylating troponin I on
                    threonine-144.
AUTHOR:             Wang H.; Grant J.E.; Doede C.M.; Sadayappan S.; Robbins J.;
                    Walker J.W.
CORPORATE SOURCE:   J.W. Walker, Department of Physiology, University of
                    Wisconsin, 1300 University Avenue, Madison, WI 53706,
                    United States. jwalker@physiology.wisc.edu
SOURCE:             Journal of Molecular and Cellular Cardiology, (2006) Vol.
                    41, No. 5, pp. 823-833. .
                    Refs: 49
                    ISSN: 0022-2828  CODEN: JMCDAY
PUBLISHER IDENT.:   S 0022-2828(06)00775-9
COUNTRY:            United Kingdom
DOCUMENT TYPE:      Journal; Article
FILE SEGMENT:       005     General Pathology and Pathological Anatomy
LANGUAGE:           English
SUMMARY LANGUAGE:   English
ENTRY DATE:         Entered STN: 16 Nov 2006
                    Last Updated on STN: 16 Nov 2006
AB   Ventricular myocytes express Gαq-coupled receptors that
     can mediate enhanced contractility by increasing the sensitivity
     of the contractile apparatus to Ca(2+).  The precise mechanisms
     underlying this change have been difficult to define, in part because
     myofilament regulatory proteins contain multiple phosphorylation
     sites for protein kinase C (PKC), protein kinase A (PKA) and
     myosin light chain kinase (
     MLCK), with potentially opposing effects.  MLCK
     increases whereas PKC and PKA have a strong tendency to decrease
     myofilament Ca(2+) sensitivity in myocardium.  Here we show in mouse
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cardiac myocytes that PKC-βII can increase Ca(2+) sensitivity of tension by a similar magnitude to MLCK but via a distinct mechanism. For PKC-βII (32)P-incorporation occurred primarily into cardiac troponin I (cTnI) and functional effects were highly dependent upon mutations in phosphorylation sites of cTnI. Replacement of serines-23/24 (PKA sites) with alanine prevented cross-phosphorylation of these sites, reduced (32)P-incorporation into cTnI by half and resulted in myofilament Ca(2+) sensitization rather than desensitization in response to PKC-βII. Replacement of three additional sites on cTnI, serines-43/45 and threonine-144, eliminated PKC-βII-mediated Ca(2+) sensitization and the remaining (32)P-incorporation into cTnI. A preference for PKC-βII phosphorylation of threonine-144 in the intact filament lattice was revealed by differential stable isotope labeling and supported by an analysis of peptide phosphorylation. The results suggest that threonine-144 within the critical inhibitory domain of cTnI represents a novel site of regulation of myofilament Ca(2+) sensitivity by PKC-βII, with possible implications for chronically stressed or diseased hearts.

L14 ANSWER 2 OF 26 MEDLINE on STN
ACCESSION NUMBER: 2006441356 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16806259
TITLE: The effect of myosin regulatory light chain phosphorylation on the frequency-dependent regulation of cardiac function.
AUTHOR: Dias Fernando A L; Walker Lori A; Arteaga Grace M; Walker John S; Vijayan Kalpana; Pena James R; Ke Yunbo; Fogaca Rosalvo T H; Sanbe Atsushi; Robbins Jeffrey; Wolska Beata M
CORPORATE SOURCE: Center for Cardiovascular Research, Department of Medicine, Section of Cardiology, University of Illinois at Chicago, 60612, USA.
CONTRACT NUMBER: R01 64209 (NHLBI)
R01 79032
T32 HL07692
SOURCE: Journal of molecular and cellular cardiology, (2006 Aug) Vol. 41, No. 2, pp. 330-9. Electronic Publication: 2006-06-30.
Journal code: 0262322. ISSN: 0022-2828.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200609
ENTRY DATE: Entered STN: 26 Jul 2006
Last Updated on STN: 30 Sep 2006
Entered Medline: 29 Sep 2006

AB Although it has been suggested that in cardiac muscle the phosphorylation level of myosin regulatory light chain (RLC) correlates with frequency of stimulation, its significance in the modulation of the force-frequency and pressure-frequency relationships remains unclear. We examined the role of RLC phosphorylation on the force-frequency relation (papillary muscles), the pressure-frequency relation (Langendorff perfused hearts) and shortening-frequency relation (isolated cardiac myocytes) in nontransgenic (NTG) and transgenic mouse hearts expressing a nonphosphorylatable RLC protein (RLC(P-)). At 22 degrees C, NTG and RLC(P-) muscles showed a negative force-frequency relation. At 32 degrees C, at frequencies above 1 Hz, both groups showed a flat force-frequency relation. There was a small increase in RLC phosphorylation in NTG muscles when the frequency of stimulation was increased from 0.2 Hz to 4.0 Hz.

However, the level of RLC phosphorylation in these isolated muscles was significantly lower compared to samples taken from NTG intact hearts. In perfused hearts, there was no difference in the slope of pressure-frequency relationship between groups, but the RLC(P-) group consistently developed a reduced systolic pressure and demonstrated a decreased contractility. There was no difference in the level of RLC phosphorylation in hearts paced at 300 and 600 bpm. In RLC(P-) hearts, the level of TnI phosphorylation was reduced compared to NTG. There was no change in the expression of PLB between groups, but expression of SERCA2 was increased in hearts from RLC(P-) compared to NTG. In isolated cardiac myocytes, there was no change in shortening-frequency relationship between groups. Moreover, there was no change in Ca(2+) transient parameters in cells from NTG and RLC(P-) hearts. Our data demonstrate that in cardiac muscle RLC phosphorylation is not an essential determinant of force- and pressure-frequency relations but the absence of RLC phosphorylation decreases contractility in force/pressure developing preparations.

L14 ANSWER 3 OF 26 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:459456 BIOSIS
DOCUMENT NUMBER: PREV200600449863
TITLE: Myosin light chain 2 into the mainstream of cardiac development and contractility.
AUTHOR(S): Moss, Richard L. [Reprint Author]; Fitzsimons, Daniel P.
CORPORATE SOURCE: Univ Wisconsin, Sch Med, Dept Physiol, 1300 Univ Ave, Madison, WI 53706 USA
rlmoss@physiology.wisc.edu
SOURCE: Circulation Research, (AUG 4 2006) Vol. 99, No. 3, pp. 225-227.
CODEN: CIRUAL. ISSN: 0009-7330.
DOCUMENT TYPE: Article
Editorial
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 2006
Last Updated on STN: 13 Sep 2006

L14 ANSWER 4 OF 26 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006578305 EMBASE
TITLE: Current issues with β(2)-adrenoceptor agonists: Pharmacology and molecular and cellular mechanisms.
AUTHOR: Anderson G.P.
CORPORATE SOURCE: G.P. Anderson, Cooperative Research Centre for Chronic Inflammatory Diseases, Department of Medicine, University of Melbourne, Parkville, Vic., Australia.
gpa@unimelb.edu.au
SOURCE: Clinical Reviews in Allergy and Immunology, (2006) Vol. 31, No. 2-3, pp. 119-130.
Refs: 79
ISSN: 1080-0549 CODEN: CRVADD
PUBLISHER IDENT.: CRIAI312119
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Dec 2006
Last Updated on STN: 6 Dec 2006

AB β(2)-Adrenoceptors are widely, almost ubiquitously, expressed . Activation of these receptors on bronchial smooth muscle by short- and long-acting β(2)-adrenoceptor agonists causes bronchodilation. Here, the β(2)-adrenoceptor is linked by the G protein, Gs, to adenylyl cyclase, which increases cyclic adenosine monophosphate (cAMP), thus activating protein kinase A, which affects calcium levels and reduces the efficiency of myosin light-chain kinase, causing relaxation.
Activation also entrains numerous acute and longer term downregulation responses affecting the number, location, and net efficiency of signaling of the receptor. Synthetic β(2)-agonists are all "partial agonists," incompletely able to optimally stimulate cAMP signal transduction. However, compared with some cells (such as mast cells) involved in exercise- induced asthma induction, airway smooth muscle is privileged in that transduction efficiency is intrinsically high and the tissue is very resistant to complete downregulation. Glucocorticosteroids have broadly beneficial interactions with β(2)-adrenoceptors. Researchers have recently discovered that the β(2)-adrenoceptor may function as a homodimer and that it can form heterodimers with both the β(1)- and β(3)- adrenoceptors, and possibly other receptors. This further complicates interpretation of the effect of β(2)-adrenoceptor polymorphisms, but it is unknown whether this occurs in humans in vivo. Researchers have known for some time that strong contraction involving receptors coupled to the Gq G protein (e.g., cholinergic and leukotriene receptors via negative biochemical crosstalk), virus infection (via uncoupling), and inflammation (via kinases) can impair relaxation. Most recently, researchers have discovered that the β(2)-adrenoceptor can also send potentially adverse signals after "atypical coupling" to Gq rather than Gs. The clinical implications of these uncouplings, crosstalk, and atypical coupling possibilities are not well-understood. .COPYRGT. Copyright 2006 by Humana Press Inc.

L14 ANSWER 5 OF 26 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005636336 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16299103
TITLE: Myosin light chain kinase and myosin phosphorylation effect frequency-dependent potentiation of skeletal muscle contraction.
AUTHOR: Zhi Gang; Ryder Jeffrey W; Huang Jian; Ding Peiguo; Chen Yue; Zhao Yingming; Kamm Kristine E; Stull James T
CORPORATE SOURCE: Department of Physiology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA.
CONTRACT NUMBER: HL26043 (NHLBI)
HL29043 (NHLBI)
T32HL007360 (NHLBI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2005 Nov 29) Vol. 102, No. 48, pp. 17519-24. Electronic Publication: 2005-11-18. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200605
ENTRY DATE: Entered STN: 1 Dec 2005
Last Updated on STN: 23 May 2006
Entered Medline: 22 May 2006

AB Repetitive stimulation potentiates contractile tension of fast-twitch skeletal muscle. We examined the role of myosin regulatory light chain (RLC) phosphorylation in this physiological response by ablating Ca(2+)/calmodulin-dependent skeletal muscle myosin light chain

kinase (MLCK) gene expression. Western blot and quantitative-PCR showed that MLCK is expressed predominantly in fast-twitch skeletal muscle fibers with insignificant amounts in heart and smooth muscle. In contrast, smooth muscle MLCK had a more ubiquitous tissue distribution, with the greatest expression observed in smooth muscle tissue. Ablation of the MYLK2 gene in mice resulted in loss of skeletal muscle MLCK expression, with no change in smooth muscle MLCK expression. In isolated fast-twitch skeletal muscles from these knockout mice, there was no significant increase in RLC phosphorylation in response to repetitive electrical stimulation. Furthermore, isometric twitch-tension potentiation after a brief tetanus (posttetanic twitch potentiation) or low-frequency twitch potentiation (staircase) was attenuated relative to responses in muscles from wild-type mice. Interestingly, the site of phosphorylation of the small amount of monophosphorylated RLC in the knockout mice was the same site phosphorylated by MLCK, indicating a potential alternative signaling pathway affecting contractile potentiation. Loss of skeletal muscle MLCK expression had no effect on cardiac RLC phosphorylation. These results identify myosin light chain phosphorylation by the dedicated skeletal muscle Ca(2+)/calmodulin-dependent MLCK as a primary biochemical mechanism for tension potentiation due to repetitive stimulation in fast-twitch skeletal muscle.

L14 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:418958 HCAPLUS
DOCUMENT NUMBER: 143:94421
TITLE: Fine-tuning in Ca2+ homeostasis underlies progression of cardiomyopathy in myocytes derived from genetically modified embryonic stem cells
AUTHOR(S): Grey, Corinne; Mery, Annabelle; Puceat, Michel
CORPORATE SOURCE: CRBM, CNRS FRE 2593, Montpellier, 34293, Fr.
SOURCE: Human Molecular Genetics (2005), 14(10), 1367-1377
CODEN: HMGEE5; ISSN: 0964-6906
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mutations of genes encoding contractile proteins are responsible for familial hypertrophic cardiomyopathies. Understanding the process of differentiation of cardiomyocytes carrying a mutated protein is a crucial step towards potential treatments of inherited cardiac disorders. Embryonic Stem (ES) cells which faithfully recapitulate in vitro the process of cardiac cell differentiation can be genetically modified to incorporate a mutation mimicking a cardiomyopathy. ES cell lines engineered to express a wild-type (MLC2vGFP) or a mutated form (R58QMLC2vGFP) of ventricular myosin light chain 2 (MLC2v) fused to GFP were differentiated into cardiomyocytes within embryoid bodies (EBs). Visualization of GFP combined with sarcomeric actinin immunofluorescence of EBs revealed that mutated MLC2v dramatically prevented myofibrillogenesis. Cardiomyocytes expressing wild-type MLC2v featured spontaneous Ca2+ spiking, but not those harboring the mutation. Expression of cardiac transcription factors Mef2c, GATAs, myocardin and Nkx2.5 was not affected by cell expression of mutated MLC2v. A dramatic decrease in expression of mRNAs encoding α-actin, MLC2a and MLC2v was observed in R58QMLC2vGFP EBs. This event was attributed to a failure of Mef2c to translocate into the nucleus, a Ca2+-dependent process. Expression in mutated cells of a constitutively active Ca2+- and calmodulin-dependent kinase II or treating EBs with ionomycin fully restored translocation of Mef2c into the nucleus and expression of mRNAs encoding sarcomeric proteins partially rescued

contractile activity of EBs. Alteration of Ca2+ homeostasis in mutated cardioblasts affects the transcriptional program of cardiac cell differentiation leading to a defect in myofibrillogenesis, and, in turn, in contractility. Genetically modified ES cells provide a unique cell model to determine abnormalities in Ca2+ homeostasis underlying progression of human cardiomyopathies.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 26 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2005417135 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16002744
TITLE: Dual serotonergic regulation of ventricular contractile force through 5-HT2A and 5-HT4 receptors induced in the acute failing heart.
AUTHOR: Qvigstad Eirik; Sjaastad Ivar; Brattelid Trond; Nunn Caroline; Swift Fredrik; Birkeland Jon Arne Kro; Krobert Kurt A; Andersen Geir Oystein; Sejersted Ole M; Osnes Jan-Bjorn; Levy Finn Olav; Skomedal Tor
CORPORATE SOURCE: Department of Pharmacology, University of Oslo, PO Box 1057 Blindern, 0316 Oslo, Norway.
SOURCE: Circulation research, (2005 Aug 5) Vol. 97, No. 3, pp. 268-76. Electronic Publication: 2005-07-07. Journal code: 0047103. E-ISSN: 1524-4571.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 6 Aug 2005
Last Updated on STN: 21 Oct 2005
Entered Medline: 20 Oct 2005

AB Cardiac responsiveness to neurohumoral stimulation is altered in congestive heart failure (CHF). In chronic CHF, the left ventricle has become sensitive to serotonin because of appearance of Gs-coupled 5-HT4 receptors. Whether this also occurs in acute CHF is unknown. Serotonin responsiveness may develop gradually or represent an early response to the insult. Furthermore, serotonin receptor expression could vary with progression of the disease. Postinfarction CHF was induced in male Wistar rats by coronary artery ligation with nonligated sham-operated rats as control. Contractility was measured in left ventricular papillary muscles and mRNA quantified by real-time reverse-transcription PCR. Myosin light chain-2 phosphorylation was determined by charged gel electrophoresis and Western blotting. Ca2+ transients in CHF were measured in field stimulated fluo-4-loaded cardiomyocytes. A novel 5-HT2A receptor-mediated inotropic response was detected in acute failing ventricle, accompanied by increased 5-HT2A mRNA levels. Functionally, this receptor dominated over 5-HT4 receptors that were also induced. The 5-HT2A receptor-mediated inotropic response displayed a triphasic pattern, shaped by temporally different activation of Ca2+-calmodulin-dependent myosin light chain kinase, Rho-associated kinase and inhibitory protein kinase C, and was accompanied by increased myosin light chain-2 phosphorylation. Ca2+ transients were slightly decreased by 5-HT2A stimulation. The acute failing rat ventricle is, thus, dually regulated by serotonin through Gq-coupled 5-HT2A receptors and Gs-coupled 5-HT4 receptors.

L14 ANSWER 8 OF 26 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004578872 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15331360
TITLE: Basal myosin light chain phosphorylation is a determinant of Ca2+

sensitivity of force and activation dependence of the kinetics of myocardial force development.

AUTHOR: Olsson M Charlotte; Patel Jitandrakumar R; Fitzsimons Daniel P; Walker Jeffery W; Moss Richard L

CORPORATE SOURCE: Dept. of Physiology, Univ. of Wisconsin Medical School, 1300 University Ave., Madison, WI 53706, USA.

CONTRACT NUMBER: HL-47053 (NHLBI)

SOURCE: American journal of physiology. Heart and circulatory physiology, (2004 Dec) Vol. 287, No. 6, pp. H2712-8. Electronic Publication: 2004-08-26. Journal code: 100901228. ISSN: 0363-6135.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200501

ENTRY DATE: Entered STN: 23 Nov 2004
Last Updated on STN: 4 Jan 2005
Entered Medline: 3 Jan 2005

AB It is generally recognized that ventricular myosin regulatory light chains (RLC) are approximately 40% phosphorylated under basal conditions, and there is little change in RLC phosphorylation with agonist stimulation of myocardium or altered stimulation frequency. To establish the functional consequences of basal RLC phosphorylation in the heart, we measured mechanical properties of rat skinned trabeculae in which approximately 7% or approximately 58% of total RLC was phosphorylated. The protocol for achieving approximately 7% phosphorylation of RLC involved isolating trabeculae in the presence of 2,3-butanedione monoxime (BDM) to dephosphorylate RLC from its baseline level. Subsequent phosphorylation to approximately 58% of total was achieved by incubating BDM-treated trabeculae in solution containing smooth muscle myosin light chain kinase, calmodulin, and Ca2+ (i.e., MLCK treatment). After MLCK treatment, Ca2+ sensitivity of force increased by 0.06 pCa units and maximum force increased by 5%. The rate constant of force development (ktr) increased as a function of Ca2+ concentration in the range between pCa 5.8 and pCa 4.5. When expressed versus pCa, the activation dependence of ktr appeared to be unaffected by MLCK treatment; however, when activation was expressed in terms of isometric force-generating capability (as a fraction of maximum), MLCK treatment slowed ktr at submaximal activations. These results suggest that basal phosphorylation of RLC plays a role in setting the kinetics of force development and Ca2+ sensitivity of force in cardiac muscle. Our results also argue that changes in RLC phosphorylation in the range examined here influence actin-myosin interaction kinetics differently in heart muscle than was previously reported for skeletal muscle.

L14 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:884183 HCAPLUS

DOCUMENT NUMBER: 142:277201

TITLE: Myosin light chain kinase knockout

AUTHOR(S): Somylo, A. V.; Wang, H.; Choudhury, N.; Khromov, A. S.; Majesky, M.; Owens, G. K.; Somlyo, A. P.

CORPORATE SOURCE: Dep. Mol. Physiol. Biol. Phys., Univ. Virginia, Charlottesville, VA, USA

SOURCE: Journal of Muscle Research and Cell Motility (2004), 25(3), 241-242
CODEN: JMRMD3; ISSN: 0142-4319

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mice showing complete lack of expression of vertebrate short and long MLCK smooth muscle isoforms and telokin were generated along with a telokin selective knockout (KO) mice. The MLCK KO mice showed a ratio of -/-:+/-:+/+ close to that expected based on Mendelian inheritance with a normal litter size of nine. However, at E14.5, 20% of the -/- embryos had deformed heads, which have also been observed in some null animals at birth. Remarkably, blood vessels at E14.5 to term from MLCK null embryos, permeabilized with alpha-toxin, developed force in response to increases in Ca2+ concns. and relaxed upon lowering calcium to pCa 7.0. Ca2+ sensitization could be induced by addition of GTPγS to muscles submaximally contracted with Ca2+ and this contraction was relaxed by the Rho-kinase inhibitor, Y-27632. Stimulation of the cultured MLCK -/- and +/+ cells with lysophosphatidic acid induced regulatory light chain (RLC) phosphorylation in both -/- and +/+ cultured aortic cells as detected by Ser19 phospho-specific RLC antibodies. Furthermore, the observed defects in the development of the coronary vessels and myocardium in the MLCK null embryos suggest a defect in the migration of the mesothelial cells of the proepicardium which around E9.5 to E10 in the mouse make contact with the heart and then extend over the surface of the myocardium to cover the heart. Results suggest that the ubiquitously expressed smooth muscle MLCK activity may be sufficient, but is not necessary for cytokinesis and early morphogenesis and that during embryonic development Ca2+-dependent kinase(s), other than the classical MLCK can phosphorylate MLC20 and induce contraction.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 26 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:123465 BIOSIS
DOCUMENT NUMBER: PREV200400126882
TITLE: Interactions between myosin light chains and cardiac troponin I phosphorylation regulate myofilament Ca2+ sensitivity in mouse myocardium.
AUTHOR(S): Wang, Hao [Reprint Author]; Walker, Jeffery W. [Reprint Author]
CORPORATE SOURCE: Physiology, University of Wisconsin, Madison, WI, USA
SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp. 210a. print.
Meeting Info.: 48th Annual Meeting of the Biophysical Society. Baltimore, MD, USA. February 14-18, 2004. Biophysical Society.
ISSN: 0006-3495 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Mar 2004
Last Updated on STN: 3 Mar 2004

AB Interactions between thick and thin filament proteins may play a critical role in the regulation of striated muscle contraction. Transgenic mice expressing non-phosphorylatable forms of the thin filament protein cardiac troponin I (cTnI) were used to investigate regulatory interactions between phosphorylation of myosin light chains and cTnI. In one set of experiments, the effects of phosphorylation of myosin regulatory light chains (MLC-2) on the Ca2+ sensitivity of isometric tension were studied in skinned ventricular myocytes. Myosin light chain kinase (MLCK) treatment induced an increase in Ca2+ sensitivity of isometric force by 0.1 pCa unit in both wild type myocytes, and in cTnI-Ala2 myocytes that could not be phosphorylated on

serines23/24 (PKA sites). In contrast, MLCK treatment had no effect on the Ca2+ sensitivity of cTnI-Ala5 myocytes that could not be phosphorylated on serines23/24 (PKA sites), serines43/45 or threonine144 (PKC sites) of cTnI. Similar levels of 32P-phosphate incorporation into MLC-2 were observed in all three mouse lines following MLCK treatment. In parallel experiments, a peptide derived from the primary sequence of myosin essential light chain (MLC-1 peptide; residues 5-14; 150 nM) increased the Ca2+ sensitivity of isometric force by 0.1 pCa unit in wild type and by 0.09 pCa unit in cTnI-Ala2 myocytes but not in cTnI-Ala5 myocytes. We propose that phosphorylation of cTnI on serines43,45 and/or threonine144 (PKC sites) is necessary to prime the thin filament regulatory system to the sensitizing influences of myosin light chains on cardiac muscle contraction. The data suggest that ensemble myofilament Ca2+ sensitivity is determined by non-additive interactions between phosphorylated thick and thin filament proteins.

L14 ANSWER 11 OF 26 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:524587 BIOSIS
DOCUMENT NUMBER: PREV200510314550
TITLE: Carboxyl-terminal fragment of myosin light chain kinase increases actin translocation velocity of cardiac muscles.
AUTHOR(S): Kato, Masayoshi [Reprint Author]; Yamashita, Hiroshi; Nishimura, Satoshi; Sugiura, Seiryo; Momomura, Shin-ichi; Chaen, Shigeru; Takano-Ohmuro, Hiromi; Kohama, Kazuhiro
CORPORATE SOURCE: Univ Tokyo, Tokyo, Japan
SOURCE: Circulation, (OCT 26 2004) Vol. 110, No. 17, Suppl. S, pp. 202-203.
Meeting Info.: 77th Scientific Meeting of the American-Heart-Association. New Orleans, LA, USA. November 07 -10, 2004. Amer Heart Assoc.
CODEN: CIRCAZ. ISSN: 0009-7322.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Dec 2005
Last Updated on STN: 1 Dec 2005

AB Background: Myosin light chain kinase (MLCK) is a multifunctional regulatory protein consisting of a putative myosin-binding site in the carboxyl terminus and a kinase domain phosphorylating the regulatory light chain (RLC) of myosin. In smooth muscles, MLCK was shown to have a non-kinase stimulatory effect, i.e., MLCK fragments containing the myosin-binding site but lacking the kinase domain increased ATPase activity of unphosphorylated myosin by directly binding to myosin heads without changing the phosphorylation level of RLC. Although similar MILCK isoform is expressed in cardiac muscles, it is not clarified whether MILCK has direct stimulatory effects on the motor function of myosin. Methods: To study the non-kinase effects of MILCK, we expressed a smooth muscle MLCK fragment (MF) containing the myosin-biding site but lacking the kinase domain in E coli. Then we measured actin-activated ATPase activity, actin translocation velocity, and unitary displacements in the presence (+) and absence (-) of MF. Actin-activated ATPase activity was determined by mixing myosin with various concentrations of actin and measuring released inorganic phosphate. Actin translocation velocity in the in vitro motility assay was measured by the method of Kron and Spudich. We also measured the unitary displacement of a single myosin molecule and actin filament suspended by a pair of microspheres using the laser optical trap system, Results: The

phosphorylation level of RLC was not affected by MF. MF did not change actin-activated ATPase activity [0.90 (-) vs. 0.90 sec(-1) (-) at actin concentration of 30 mu M]. However, the translocation velocity of actin was significantly higher in the presence of MF [5.6 +/- 0.5 (+) vs. 4.6 +/- 0.4 mu m/s (-), p < 0.01]. The MF didn't alter the unitary displacement [9.3 +/- 0.5 (+) vs 9.8 +/- 0.3 nm (-), N.S.] suggesting that the difference in translocation velocity was induced by the change in kinetics of actin-myosin interaction. Conclusion: In cardiac muscles, MLCK may directly modulate mechanical interaction of actin and myosin by non-kinase activity in addition to the Ca2+-sensitizing effect by phosphorylating the light chain, thus play a significant role in the regulation of cardiac muscle contraction.

L14 ANSWER 12 OF 26 EMBASE

ACCESSION NUMBER: 2004507711 EMBASE

TITLE: Basal myosin light chain phosphorylation is a determinant of Ca (2+) sensitivity of force and activation dependence of the kinetics of myocardial force development.

AUTHOR: Olsson M.C.; Patel J.R.; Fitzsimons D.P.; Walker J.W.; Moss R.L.

CORPORATE SOURCE: J.R. Patel, Dept. Physiology, Univ. of Wisconsin Medical School, 1300 University Ave., Madison, WI 53706, United States. jrpatel@physiology.wisc.edu

SOURCE: American Journal of Physiology - Heart and Circulatory Physiology, (2004) Vol. 287, No. 6 56-6, pp. H2712-H2718. Refs: 49
ISSN: 0363-6135 CODEN: AJPPDI

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 28 Dec 2004
Last Updated on STN: 28 Dec 2004

AB It is generally recognized that ventricular myosin regulatory light chains (RLC) are .apprx.40% phosphorylated under basal conditions, and there is little change in RLC phosphorylation with agonist stimulation of myocardium or altered stimulation frequency. To establish the functional consequences of basal RLC phosphorylation in the heart, we measured mechanical properties of rat skinned trabeculae in which .apprx.7% or .apprx.58% of total RLC was phosphorylated. The protocol for achieving .apprx.7% phosphorylation of RLC involved isolating trabeculae in the presence of 2,3-butanedione monoxime (BDM) to dephosphorylate RLC from its baseline level. Subsequent phosphorylation to .apprx.58% of total was achieved by incubating BDM-treated trabeculae in solution containing smooth muscle myosin light chain kinase, calmodulin, and Ca(2+) (i.e., MLCK treatment). After MLCK treatment, Ca(2+) sensitivity of force increased by 0.06 pCa units and maximum force increased by 5%. The rate constant of force development (k(tr)) increased as a function of Ca(2+) concentration in the range between pCa 5.8 and pCa 4.5. When expressed versus pCa, the activation dependence of k(tr) appeared to be unaffected by MLCK treatment; however, when activation was expressed in terms of isometric force-generating capability (as a fraction of maximum), MLCK treatment slowed k(tr) at submaximal activations. These results suggest that basal phosphorylation of RLC plays a role in setting the kinetics of force development and Ca(2+) sensitivity of force in cardiac muscle. Our results also argue that changes in RLC phosphorylation in the range examined here

influence actin-myosin interaction kinetics differently in heart muscle than was previously reported for skeletal muscle.

L14 ANSWER 13 OF 26 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:291514 BIOSIS
DOCUMENT NUMBER: PREV200400290996
TITLE: A Myosin Light Chain Kinase (MLCK) Knockout.
AUTHOR(S): Wang, Hua [Reprint Author]; Somlyo, Andrew P; Somlyo, Avril
CORPORATE SOURCE: Molecular Physiology and Biological Physics, University of Virginia, 1300 Jefferson Park Ave, Charlottesville, Va, 22903, USA
hw2p@virginia.edu
SOURCE: FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst. 699.22. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia, USA. April 17-21, 2004. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jun 2004
Last Updated on STN: 23 Jun 2004

AB Short (130kDa) and long (220kDa) MLCK isoforms of vertebrate smooth muscle and telokin are products of a single gene. Smooth muscle MLCK transcripts are ubiquitously expressed and regulate, Ca-calmodulin dependently, smooth muscle and non-muscle myosin II. In generating a telokin null mouse by homologous recombination, the targeted KO vector flanked by loxP sites inserted in the telokin promoter region of MLCK resulted in embryonic lethals that survived up to E16.5. 15 litters (mean litter size of 9) at E14.5 had 26 -/- embryos, 7 of which had deformed heads, but no gross anatomical phenotype of heart, blood vessel or gut. Western blots of the stomach and intestines of -/- animals showed absence of both long and short MLCK and telokin; skeletal MLCK was not detected nor were major differences in ROKa, ROKb, PAK or citron kinase expression. a-toxin permeabilized E14.5 aortas contracted in response to Ca2+ and could be Ca2+ -sensitized with GTPgS, reversibly by Rho-kinase inhibitor, Y-27362. MLC20 phosphorylation was detectable in intact -/- gastric smooth muscle stimulated with carbachol. Our results suggest that the ubiquitously expressed smooth muscle MLCK activity may be sufficient, but is not necessary, for cytokinesis and early morphogenesis and that during embryonic development Ca2+-dependent kinase(s), other than the classical MLCK, can phosphorylate MLC20 and induce contraction. .

L14 ANSWER 14 OF 26 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003150919 EMBASE
TITLE: Regulation of force in vascular smooth muscle.
AUTHOR: Ogut O.; Brozovich F.V.
CORPORATE SOURCE: F.V. Brozovich, Dept. of Physiology and Biophysics, Case W. Reserve Univ. Sch. of Med., 10900 Euclid Avenue, Cleveland, OH 44106-4970, United States. fxb9@po.cwru.edu
SOURCE: Journal of Molecular and Cellular Cardiology, (1 Apr 2003) Vol. 35, No. 4, pp. 347-355. .
Refs: 95
ISSN: 0022-2828 CODEN: JMCDAY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 002 Physiology

029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Apr 2003
Last Updated on STN: 24 Apr 2003

AB Vascular smooth muscle contraction plays a defining role in the regulation and maintenance of blood pressure, and its deregulation is associated with many clinical syndromes including hypertension, coronary vasospasm and congestive heart failure. Over the past 20 years, there has been a growing understanding of the regulation of 20 kDa myosin light chain phosphorylation by myosin light chain kinase and myosin light chain phosphatase, the role of splice-variant isoforms of both the myosin heavy chain and the essential myosin light chain, as well as the signaling pathways involved in smooth muscle contraction under normal and pathophysiological conditions. This review will attempt to recapitulate the data in the field, primarily focusing on the contractile response of smooth muscle, and the molecular determinants responsible for the regulation of vascular tone.

L14 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:240950 HCAPLUS
DOCUMENT NUMBER: 136:274318
TITLE: Optimized cardiac contraction through differential phosphorylation of myosin by modulation of the human cardiac isoform of myosin light chain kinase
INVENTOR(S): Epstein, Neal D.; Hassanzadeh, Shahin; Winitsky, Steven; Davis, Julien S.
PATENT ASSIGNEE(S): The Government of the United States of America, as Represented by the Secretary, Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002024889	A2	20020328	WO 2001-US28639		20010912
WO 2002024889	A3	20030904			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004126860	A1	20040701	US 2003-380236		20030925
PRIORITY APPLN. INFO.:			US 2000-232246P	P	20000912
			US 2000-232456P	P	20000913
			WO 2001-US28639	W	20010912

AB The present disclosure provides a cDNA, protein sequence, and genomic structure of the human cardiac isoform of myosin light chain kinase (cMLCK), and described mutations in the cMLCK gene that are associated with cardiac

dysfunction. Methods are provided for identifying individuals who can harbor mutations in the cMLCK gene, or carry alleles that can predisposed them to cardiac dysfunction. Disclosed also is a significant role for cMLCK in modulating cardiac contractility. The cMLCK protein is shown to reduce the amplitude of stretch activation and increase the tension production, a property of muscle which has heretofore had an unknown role in cardiac contraction. Moreover, the cMLCK protein is shown to be regionally distributed in the heart, thereby having differential effects on contractility and stretch activation. Methods herein are provided to exploit this effect of cMLCK, to treat individuals who have or are prone to cardiac dysfunction. In addition, methods are provided to identify agents that modulate cMLCK activity, thereby having potential therapeutic importance in the treatment of cardiac dysfunction.

L14 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:65948 HCAPLUS
DOCUMENT NUMBER: 139:258419
TITLE: A "wringing" endorsement for myosin phosphorylation in the heart
AUTHOR(S): Vandenboom, Rene; Metzger, Joseph M.
CORPORATE SOURCE: Department of Physiology, University of Michigan, Ann Arbor, MI, 48109, USA
SOURCE: Molecular Interventions (2002), 2(7), 422-424
CODEN: MIONAR; ISSN: 1534-0384
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review examines the physiol. significance of the cardiac protein phosphorylation in vivo in both myosin light chain kinase expression and activity across the myocardium. A study by Davis et al. (2001) showed that in addition to an increase Ca2+ sensitivity, R-LC phosphorylation alters the stretch activation response in which the biphasic tension rise that occurs when a contracting muscle is lengthened. Phosphorylation of cardiac-like slow-twitch fibers decrease the difference between the tension mania that occur when the initial, rapid tension transient relaxes and the tension maxima that occur during the peak of the delayed, slower transient that follows. This dampened contractile response could result from the altered rate at which cycling cross-bridges are able to regenerate tension after perturbation by stretch. R-LC phosphorylation mediated modulations of the stretch-activation response may have important implication for the heart, where oscillatory work is performed on a beat-by-beat basis. Davis et al. also showed that a skeletal like-MLCK is expressed in spatially-specific manner across the myocardium, decreasing from the apex to the mind ventricle region as well as across te heart wall, from the epicardium. Evidence that the MLCK is active in the heart is provided by the patten of R-LC phosphorylation, which corresponds to the pattern of MLCK expression.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 17 OF 26 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003063750 EMBASE
TITLE: A molecular mechanism improving the contractile state in human myocardial hypertrophy.
AUTHOR: Ritter O.; Bottez N.; Burkard N.; Schulte H.D.; Neyses L.
CORPORATE SOURCE: Dr. L. Neyses, University Department of Medicine, Manchester Heart Centre, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL, United Kingdom.

ludwig.neyses@mhc.cmht.nwest.nhs.uk
SOURCE: Experimental and Clinical Cardiology, (2002) Vol. 7, No. 2-3, pp. 151-157. .
Refs: 39
ISSN: 1205-6626 CODEN: ECCAF7
COUNTRY: Canada
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Feb 2003
Last Updated on STN: 20 Feb 2003
AB Background: Various molecular mechanisms are operative in altering the sarcomeric function of the heart under increased hemodynamic workload. Expression of the atrial isoform (ALC-1) of the essential myosin light chain, a shift from α-myosin heavy chain (MHC) to β-MHC, increased phosphorylation of the regulatory myosin light chains and increased troponin I (TnI) phosphorylation have been reported to modulate cardiac contractility in rodents. Methods: To assess a possible contribution of these sarcomeric proteins to cardiac performance in human myocardial hypertrophy, two different forms of cardiac hypertrophy were investigated: 19 patients with hypertropic obstructive cardiomyopathy (HOCM) and 13 patients with aortic stenosis (AS) with marked left ventricular hypertrophy and normal systolic function. Results: There was no change in MHC gene expression, regulatory myosin light chain or TnI phosphorylation status in normal heart (NH), HOCM and AS patients. However, patients with hypertrophied myocardium expressed ALC-1 that was not detectable in NH. ALC-1 protein expression correlated positively with the left ventricular ejection fraction. In patients with hypertrophied myocardium, there was a mean ALC-1 protein expression of 12.7±3% (range 3.6% to 32%). Conclusion: In humans, ALC-1 expression is in vivo a powerful molecular mechanism of the sarcomere to maintain or improve myocardial contractility under increased hemodynamic demands.

L14 ANSWER 18 OF 26 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:122165 SCISEARCH
THE GENUINE ARTICLE: 624ZK
TITLE: Isoproterenol induced changes of protein expression and myocardial ultrastructure
AUTHOR: Dudnakova T V (Reprint); Lakomkin V; Tsyplenkova V G; Shekhonin B V; Shirinsky V P; Kapelko V I
CORPORATE SOURCE: Russian Cardiol Sci Ind Complex, 3rd Cherepkovskaya 15A, Moscow 121552, Russia (Reprint); Russian Cardiol Sci Ind Complex, Moscow 121552, Russia
COUNTRY OF AUTHOR: Russia
SOURCE: KARDIOLOGIYA, (2002) Vol. 42, No. 11, pp. 57-63.
ISSN: 0022-9040.
PUBLISHER: IZD VO MEDITSINA, PETROVERIGSKII PER 6-8, K-142 MOSCOW, RUSSIA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: Russian
REFERENCE COUNT: 32
ENTRY DATE: Entered STN: 14 Feb 2003
Last Updated on STN: 14 Feb 2003
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Aim. To elucidate alterations. in myocardial ultrastructure and protein expression caused by isoproterenol. Methods.

Biochemical, immunohistochemical and electron microscopic studies of rat myocardium were carried out 2 hours and 3 weeks after single injections of isoproterenol (50 and 10 mg/kg). Relative content of myospecific. proteins (KRP - kinase-related protein, desmin), cytoskeletal proteins (tubulin, vinculin, and myosin light chain kinase - MLCK) and extracellular matrix protein, fibronectin, was. determined by immunoblotting. Results. In 2 hours after injection of 50 mg/kg of isoproterenol destruction of some cardiomyocytes, contracture of myofibrils, and mild edema of intercellular space occurred; the content of KRP decreased. by 16%, and that of tubulin, vinculin and fibronectin - by 27-29%. Reduced level of these proteins and also of MLCK persisted until 3 weeks after - injection arid was associated with altered cardiomyocyte ultrastructure. Glycogen granules were sparse, mitochondria contained arrow-like inclusions characteristic for calcium overload, huge mitochondria connected by specialized intermitochondrial contacts were present. Enlarged intercellular space contained areas of fibrosis with increased amount of type I and II collagens and fibronectin. Lower dose of isoproterenol (10 mg/kg) did not cause noticeable damaging action in the acute, period, but in 3 weeks thickening of extracellular matrix occurred accompanied by increases of KRP and tubulin contents (by 26-32% compared with control level). Similar rise in expression of these proteins, and also of MLCK was observed after addition of isoproterenol to culture of chicken cardiomyocytes. Conclusion. These results indicate that even single injection of isoproterenol causes long lasting structural alterations-in cardiac muscle accompanied by increased expression of extracellular matrix proteins as well as sarcoplasmic proteins, apparently involved in the hypertrophic response of the cardiomyocytes.

L14 ANSWER 19 OF 26 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:63841 HCAPLUS
DOCUMENT NUMBER: 134:125947
TITLE: Cardiovascular active peptide and agents increasing the degree of phosphorylation of myosin for treating cardiac diseases
INVENTOR(S): Haase, Hannelore; Morano, Ingo
PATENT ASSIGNEE(S): Max-Delbruck-Centrum fur Molekulare Medizin, Germany
SOURCE: PCT Int. Appl., 8 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001005419	A2	20010125	WO 2000-DE2342		20000717
WO 2001005419	A3	20010329			
W: JP, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
DE 10035098	A1	20010517	DE 2000-10035098		20000717
PRIORITY APPLN. INFO.:			DE 1999-19933090	A	19990715
			DE 1999-19938255	A	19990812

AB An agent for treating cardiac diseases is disclosed. More particularly, the invention discloses a cardiovascular-active peptide, as well as substances which increase the degree of phosphorylation of myosin, especially the MLC-2 chain thereof. The invention is applicable in medicine and the pharmaceutical industry. The agent for treating cardiac diseases contains peptides which imitate the calcium channel α1 subunit interaction domain, or substances which increase the degree of phosphorylation of myosin, especially the MLC-2 chain thereof. According to the first embodiment of the invention, a peptide is

synthesized which imitates the calcium channel α1 subunit interaction domain which is expressed in vascular muscle and heart (α1C). The peptide is known as a cAIP (cardiac-type α1 interaction peptide). The amino acid sequence is: QQLEEDLKGYLDWITQAE. The other embodiment of the invention involves an increase of in vivo phosphorylation of MLC-2 and thus an improvement in the contractility of the human heart.

L14 ANSWER 20 OF 26 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001687027 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11733062
TITLE: The overall pattern of cardiac contraction depends on a spatial gradient of myosin regulatory light chain phosphorylation.
AUTHOR: Davis J S; Hassanzadeh S; Winitsky S; Lin H; Satorius C; Vemuri R; Aletras A H; Wen H; Epstein N D
CORPORATE SOURCE: Molecular Physiology Section, Cardiology Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD 20892, USA.
SOURCE: Cell, (2001 Nov 30) Vol. 107, No. 5, pp. 631-41. Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF325549
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 5 Dec 2001
Last Updated on STN: 24 Jan 2002
Entered Medline: 28 Dec 2001

AB Evolution of the human heart has incorporated a variety of successful strategies for motion used throughout the animal kingdom. One such strategy is to add the efficiency of torsion to compression so that blood is wrung, as well as pumped, out of the heart. Models of cardiac torsion have assumed uniform contractile properties of muscle fibers throughout the heart. Here, we show how a spatial gradient of myosin light chain phosphorylation across the heart facilitates torsion by inversely altering tension production and the stretch activation response. To demonstrate the importance of cardiac light chain phosphorylation, we cloned a myosin light chain kinase from a human heart and have identified a gain-in-function mutation in two individuals with cardiac hypertrophy.

L14 ANSWER 21 OF 26 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 1999023816 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9806740
TITLE: Expression of a novel high molecular-weight myosin light chain kinase in endothelium.
AUTHOR: Verin A D; Lazar V; Torry R J; Labarrere C A; Patterson C E; Garcia J G
CORPORATE SOURCE: Department of Medicine, Physiology and Biophysics, Indiana University School of Medicine, Indianapolis, Indiana, USA.
CONTRACT NUMBER: HL50533 (NHLBI)
HL57462 (NHLBI)
HL58064 (NHLBI)
SOURCE: American journal of respiratory cell and molecular biology, (1998 Nov) Vol. 19, No. 5, pp. 758-66. Journal code: 8917225. ISSN: 1044-1549.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 15 Jan 1999
Last Updated on STN: 15 Jan 1999
Entered Medline: 23 Dec 1998

AB Myosin light chain phosphorylation results in cellular contraction and is a critical component of agonist-mediated endothelial cell (EC) junctional gap formation and permeability. We have shown that this reaction is catalyzed by a novel high molecular-weight Ca2+/calmodulin-dependent nonmuscle myosin light chain kinase (MLCK) isoform recently cloned in human endothelium (Am. J. Respir. Cell Mol. Biol., 1997;16:489-494). To characterize EC MLCK expression further in cultured and adult tissues, we employed immunoblotting techniques and reverse transcriptase-polymerase chain reaction to demonstrate that freshly isolated and cultured human macro- and microvascular EC express only the EC MLCK isoform (214 kD), which is distinct from smooth-muscle MLCK isoforms (130 to 150 kD). Immunocytochemical studies demonstrated the presence of the high molecular-weight MLCK isoform in adult human cardiac endothelium using anti-MLCK antibodies, which preferentially recognize the high molecular-weight EC MLCK isoform. Monitoring of MLCK expression in different cell types with antibodies generated against a unique human EC MLCK N-terminal sequence revealed a high level of expression of the 214-kD enzyme in endothelium, minimal level of expression in smooth muscle, and no expression in skeletal muscle. These data suggest that the novel 214-kD kinase, the only MLCK isoform found in endothelium, may be preferentially expressed in this nonmuscle tissue.

L14 ANSWER 22 OF 26 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:33717 HCAPLUS
DOCUMENT NUMBER: 128:100577
TITLE: Myosin light chain phosphatase and kinase abnormalities in fetal sheep pulmonary hypertension
AUTHOR(S): Belik, Jaques; Majumdar, Ramanath; Fabris, Viciany E.; Kerc, Ewa; Pato, Mary D.
CORPORATE SOURCE: Department of Pediatrics, University of Calgary, Calgary, AB, T2N 2T9, Can.
SOURCE: Pediatric Research (1998), 43(1), 57-61
CODEN: PEREBL; ISSN: 0031-3998
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Inasmuch as smooth muscle contractile protein abnormalities may account for the maintenance of a high pulmonary vascular resistance, the authors evaluated the pulmonary arterial myosin light chain kinase (MLCK) and phosphatase (MLCP) in normal and pulmonary hypertensive (PH) fetal sheep. In addition, aorta and vena cava MLCP and MLCK activities were also measured. The MLCK activity (nanomoles/min/mg) was determined by the incorporation of [32P]PO4-3 into the 20 kDa smooth muscle myosin light chains and the MLCP activity by assaying for the dephosphorylation of the 20 kDa myosin light chain (MLCP-light chain) and heavy meromyosin (MLCP-HMM). The MLCP content was determined by Western blot anal. PH was characterized by a significant increase in the right-to-left ventricular wall weight ratio from 0.99 in the control to 1.52 in the exptl. group. The pulmonary MLCP-light chain and MLCP-HMM activities in the exptl. group

were 2.0 and 1.3 and significantly lower than in the control group values (3.8 and 2.5). The MLCK activity was 9.6 in the control and 7.8 in the exptl. fetal pulmonary artery (p = NS). The activities of both enzymes in the aorta and vena cava samples were not altered by PH. The MLCP content in exptl. animals (0.50 OD + mm2) was significantly lower than that for the control pulmonary tissue (1.72), suggesting that PH down-regulates pulmonary vascular MLCP expression. In conclusion, the maintenance of a high pulmonary vascular resistance in PH may be secondary to abnormalities in tissue content and/or activity of MLCP.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 23 OF 26 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1997:400925 SCISEARCH
THE GENUINE ARTICLE: XA411
TITLE: Smooth muscle myosin light chain kinase is transiently expressed in skeletal muscle during embryogenesis and muscle regeneration both in vivo and in vitro
AUTHOR: DallaLibera L (Reprint); PodhorskaOkolow M; Martin B; Massimino M L; Brugnolo R; Cantini M
CORPORATE SOURCE: UNIV PADUA, DEPT BIOMED SCI, CNR, UNIT MUSCLE BIOL & PHYSIOPATHOL, VIA TRIESTE 75, I-35131 PADUA, ITALY (Reprint); MED ACAD WROCLAW, DEPT HISTOL, PL-50386 WROCLAW, POLAND
COUNTRY OF AUTHOR: ITALY; POLAND
SOURCE: JOURNAL OF MUSCLE RESEARCH AND CELL MOTILITY, (JUN 1997) Vol. 18, No. 3, pp. 295-303.
ISSN: 0142-4319.
PUBLISHER: CHAPMAN HALL LTD, 2-6 BOUNDARY ROW, LONDON, ENGLAND SE1 8HN.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 42
ENTRY DATE: Entered STN: 1997
Last Updated on STN: 1997

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB By using a polyclonal antibody raised against smooth muscle Myosin Light Chain Kinase of adult chicken we show that the 135 kDa smooth muscle Myosin Light Chain Kinase isoform is present in neonatal and regenerating rat skeletal muscle, as well as in adult atrial myocardium. No reaction was evident in adult skeletal muscle fibres. In neonatal and in early regenerating muscle smooth muscle Myosin Light Chain Kinase is associated with embryonic myosin as revealed by their co-presence in muscle fibres. Experiments in vitro show the same results in myotubes. In atrial myocardium there is a patchy positivity in certain group of myocytes. Immunoblotting experiments show in muscle cell cultures, in neonatal and in regenerating skeletal muscle a protein band with electrophoretic mobility corresponding to that of smooth muscle Myosin Light Chain Kinase. These results suggest that the expression of smooth muscle Myosin Light Chain Kinase is not fully tissue-specific and that regulation of the contractile machinery could be different during myogenesis and in adulthood, in relation to the peculiar dynamic characteristics ol: developing muscles.

L14 ANSWER 24 OF 26 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on

STN DUPLICATE 7

ACCESSION NUMBER: 1994:105966 BIOSIS
DOCUMENT NUMBER: PREV199497118966
TITLE: Probing the regulation of contractility in cardiac and smooth muscle skinned fibers with synthetic peptides.
AUTHOR(S): Strauss, John D.; Barth, Zacharias; Van Eyk, Jennifer E.; Ruegg, J. Caspar
CORPORATE SOURCE: II Physiologisches Inst., Univ. Heidelberg, INF 326, D-69120 Heidelberg, Germany
SOURCE: Methods (Orlando), (1993) Vol. 5, No. 3, pp. 281-290. CODEN: MTHDE9. ISSN: 1046-2023.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Mar 1994
Last Updated on STN: 15 Mar 1994

AB Methods for using synthetic peptides to specifically probe the molecular mechanisms for calcium-dependent regulation of contraction in cardiac and smooth permeabilized (or skinned) muscle are described. As examples of the use of these tools, the role of troponin in modulating the cardiac crossbridge cycle and the regulatory action of myosin light chain kinase (MLCK) in smooth muscle In Triton X-100-extracted muscle preparations have been targeted. These "skinned" fibers are functional in terms of contractility but permit precise control of aspects of the "cytoplasmic" environment around the myofilaments, such as calcium and substrate concentration. They also permit the diffusion of peptides into the "intracellular" compartment. These include peptides derived from the common actin-binding, troponin C-binding sequence of troponin I (the so-called inhibitory sequence, Tnl 104-115) and the calmodulin-binding sequence of MLCK (also known as RS20). The effects of these peptides were monitored in terms of changes in isometric tension and expressed as changes in calcium or calmodulin sensitivity. The calmodulin-binding peptide reduced force at a fixed calcium concentration, indicating decreased calcium sensitivity. This effect was associated with a moderate decrease in myosin fight chain phosphorylation and could be reversed with increased calmodulin concentration. We interpret this latter observation to mean that underlying the change in apparent calcium sensitivity is a change in the sensitivity of MLCK to calmodulin. As previously reported, the troponin I-based peptide desensitizes skinned cardiac muscle with respect to calcium by inhibiting the actin activation of the crossbridge cycle. We also discuss the results of recent experiments in which this peptide was used in conjunction with a calcium-sensitizing compound, EMD 53998. These results implicate the phosphate release step as the most likely regulatory step in the crossbridge cycle affected by the peptide and, by extension, troponin I. Peptide studies such as these have provided useful specific insights into the highly complex and multivariable regulatory systems of contraction.

L14 ANSWER 25 OF 26 EMBASE

ACCESSION NUMBER: 92175408 EMBASE
DOCUMENT NUMBER: 1992175408
TITLE: Effects of different expression and posttranslational modifications of myosin light chains on contractility of skinned human cardiac fibers.
AUTHOR: Morano I.
CORPORATE SOURCE: II, Physiologisches Institut, Universitat Heidelberg, Im Neuenheimer Feld 326,6900 Heidelberg, Germany
SOURCE: Basic Research in Cardiology, (1992) Vol. 87, No. SUPPL. 1, pp. 129-141. .

ISSN: 0300-8428 CODEN: BRCAB7
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Jul 1992
Last Updated on STN: 5 Jul 1992

AB In the human ventricle two isoforms of the phosphorylatable myosin light chain (MPLC) are expressed. These two forms are designated with increasing acidity as LC-2 and LC-2(*). In the normal human heart the relation between LC-2/LC-2(*)-expression is 70/30, suggesting the existence of three different myosin isoenzymes (MPLC-polymorphism) in the normal human ventricle. Both ventricular MPLC-iso forms are monophosphorylated, the LC-2 being higher phosphorylated than the LC-2(*). In some patients with heart failure both MPLC isoforms were found to be completely dephosphorylated. In the human atrium a MPLC isoform is expressed which is different from the ventricular MPLC isoforms. The atrial MPLC isoform is mono- and diphosphorylated. Mono-phosphorylation of both the ventricular MPLC isoforms and the atrial MPLC isoform increased responsiveness as well as sensitivity of isometric tension generation of skinned fibers to Ca2+. Part of this effect could be explained by changing the cross-bridge-cycling rate: MPLC increased f(app), the rate-constant for the transition of cross-bridges from the non-force into the force-generating state, thus increasing the amount of force-generating cross-bridge states at a given [Ca2+]. Monophosphorylation of the MPLC isoforms did not change maximal shortening velocity.

L14 ANSWER 26 OF 26 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 92206342 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1372785
TITLE: Pharmacology of bepridil.
AUTHOR: Gill A; Flaim S F; Damiano B P; Sit S P; Brannan M D
CORPORATE SOURCE: Department of Cardiovascular Pharmacology, R.W. Johnson Pharmaceutical Research Institute, Spring House, Pennsylvania.
SOURCE: The American journal of cardiology, (1992 Apr 9) Vol. 69, No. 11, pp. 11D-16D. Ref: 36
Journal code: 0207277. ISSN: 0002-9149.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 9 May 1992
Last Updated on STN: 29 Jan 1996
Entered Medline: 27 Apr 1992

AB Bepridil is an antianginal agent with multiple therapeutic actions. It decreases calcium influx through potential-dependent and receptor-operated sarcolemmic calcium channels and acts intracellularly as a calmodulin antagonist and calcium sensitizer. Thus, in cardiac muscle it enhances the sensitivity of troponin C to calcium, stimulates myofibrillar adenosine triphosphatase activity, removes calmodulin's inhibitory effect on sarcoplasmic reticulum calcium release, and inhibits sodium-calcium exchange--actions that tend to offset the effects of calcium influx blockade on cardiac contractile force. However, in vascular smooth muscle where the calcium-calmodulin complex promotes muscle contraction by activating myosin light-

chain kinase phosphorylation of
contractile proteins, calmodulin antagonism, coupled with
bepridil's blockade of calcium influx, leads to vasorelaxation. In animal
models of ischemia, bepridil and other calmodulin inhibitors show
antiarrhythmic efficacy following reperfusion. Additionally, interfering
with calmodulin's role in sympathetic nerve terminal function may help to
limit the ischemia-induced catecholamine release that contributes to
arrhythmogenesis. Bepridil shows a lidocaine-like fast kinetic block of
inward sodium current (as distinct from the slow or intermediate kinetic
inhibition expressed by encainide or quinidine, respectively).
This inhibition is pH-dependent; activity is expressed to a
greater degree at lower pH levels. This, this potentially antiarrhythmic
mechanism is activated by conditions of ischemia. Bepridil's blockade of
outward potassium currents and its inhibition of sodium-calcium exchange
increase action potential duration and ventricular refractoriness, prolong
the QT interval, and form the basis for a class III antiarrhythmic
mechanism. Because hypokalemia also prolongs the QT interval, the
addition of bepridil in the presence of hypokalemia can lead to excessive
prolongation. Bepridil both increases myocardial oxygen supply through
coronary vasodilation and decreases myocardial oxygen demand through mild
heart rate and afterload reduction, and shows potential
antiarrhythmic activity through class IB, III, and IV mechanisms.(ABSTRACT
TRUNCATED AT 250 WORDS)

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E1            1     CHEN QX/AU
E2            5     CHEN QY/AU
E3         4492 --> CHEN R/AU
E4           34     CHEN R A/AU
E5            4     CHEN R A J/AU
E6          157     CHEN R B/AU
E7          508     CHEN R C/AU
E8           28     CHEN R C A/AU
E9            5     CHEN R C C/AU
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E12           4     CHEN R C M/AU

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L15        4492 "CHEN R"/AU

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E5            2     RUIHUA H/AU
E6            1     RUIHUA HUANG/AU
E7            1     RUIHUA JI/AU
E8            2     RUIHUA L/AU
E9            1     RUIHUA LI/AU
E10           2     RUIHUA LIU/AU
E11           2     RUIHUA NIU/AU
E12           1     RUIHUA Q/AU

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E7            2     HALLING BLAKE/AU
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L16          60 ("HALLING B P"/AU OR "HALLING BLAIK"/AU OR "HALLING BLAIK P"/AU
                OR "HALLING BLAIK PHILLIP"/AU)

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E2            5      YUHAS C M/AU
E3           29 --> YUHAS D/AU
E4           29      YUHAS D A/AU
E5           56      YUHAS D E/AU
E6            3      YUHAS DAVID A/AU
E7            1      YUHAS DEBBIE/AU
E8            2      YUHAS DEBRA/AU
E9           10      YUHAS DEBRA A/AU
E10           1      YUHAS DONALD/AU
E11           9      YUHAS DONALD E/AU
E12           2      YUHAS DONALD EUGENE/AU

=> s e6-e9
L17          16 ("YUHAS DAVID A"/AU OR "YUHAS DEBBIE"/AU OR "YUHAS DEBRA"/AU OR
                "YUHAS DEBRA A"/AU)

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E6            5      ALLEON A M/AU
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E8            3      ALLEON G/AU
E9            1      ALLEON J/AU
E10           3      ALLEONI A C C/AU
E11           1      ALLEONI ANA CLAUDIA CARRARO/AU
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=> s e4
L18          19 "ALLENZA PAUL"/AU

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=> e3-e7
E3-E7 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).
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=> s e3-e7
L19          24 ("CHAGUTURU M K"/AU OR "CHAGUTURU MUNIRATHAM K"/AU OR "CHAGUTURU
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               "CHAGUTURU MUNIRATHNAM KRISHNAPPA"/AU)

=> d his

     (FILE 'HOME' ENTERED AT 12:23:13 ON 19 JAN 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:23:44 ON 19 JAN 2007
L1         14613 S MYOSIN (3W) KINASE?
L2          4033 S "MLCK"
L3         14977 S L1 OR L2
L4       8131756 S CLON? OR EXPRESS? OR RECOMBINANT
L5          3086 S L3 AND L4
L6        134078 S LIGHT (W)CHAIN
L7          2626 S L5 AND L6
L8          4169 S APHIS (W) GOSSYPII
L9             1 S L7 AND L8
L10         1431 S L7 AND MUSCLE?
L11          651 S CONTRACT? AND L10
L12          463 S PHOSPHORYLAT? AND L11
L13           47 S L12 AND (CARDIAC OR HEART)
L14           26 DUP REM L13 (21 DUPLICATES REMOVED)
                 E CHEN R/AU
L15         4492 S E3
                 E RUIHUA C/AU
                 E HALLING B P/AU
L16           60 S E3-E6
                 E YUHAS D/AU
L17           16 S E6-E9
                 E ALLENZA P/AU
L18           19 S E4
                 E CHAGUTURU M K/AU
L19           24 S E3-E7

=> s l15 or l16 or l17 or l18 or l19
L20         4599 L15 OR L16 OR L17 OR L18 OR L19

=> s l7 and l20
L21            2 L7 AND L20

=> d 1-2 ibib ab

L21   ANSWER 1 OF 2  BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-13992  BIOTECHDS
TITLE:            New nucleic acid molecule encoding hemipteran myosin
                  light chain kinase, useful in
                  identifying or developing compounds with activity as
                  pesticides or as pharmaceuticals;
                     vector-mediated gene transfer and expression in
                     host cell for strain improvement and amino acid
                     preparationrecombinant mutant @Corynebacterium glutanicum@
                     construction, plasmid-mediated 6-@phosphogluconate-
                     dehydrogenasegene@ transfer, expression in host
                     cell, ionexchange chromatography, appl. @strain
                     improvement@, L-@lysine@, L-@threonine@, L-@isoleucine@,
                     L-@tryptophan@ prepare, human medicine, animal nutrition,
                     foodstuff manufacturemaize tissue culture and propagation
                     for plant breeding and transgenic plant constructionhybrid
                     @maize@, hybrid seed construction, protoplast culture,
                     leaf culture, pollen culture, embryo culture, root
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culture, root tip culture, anther culture, silk culture, flower culture, kernel culture, ear culture, cob culture, husk culture, stalk culture, @propagation@, @herbicide resistance@, insect @disease-resistance@ transgene, regulatory element-linked transgene, recurrent selection, backcrossing, pedigree breeding, restriction fragment length polymorphism enhanced selection, genetic marker enhanced selection, transformation, appl. @plant breeding@, @transgenic plant@ construction, human food, livestock feed, raw materialvector-mediated gene transfer and expression in host cell for recombinant protein production and pesticide screening or drug screening

AUTHOR: CHEN R; CHAGUTURU M K; YUHAS D; ALLENZA P; HALLING B P
PATENT ASSIGNEE: FMC CORP
PATENT INFO: WO 2004029577 8 Apr 2004
APPLICATION INFO: WO 2003-US29901 18 Sep 2003
PRIORITY INFO: US 2002-413720 26 Sep 2002; US 2002-413720 26 Sep 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-340457 [31]

AB DERWENT ABSTRACT:
NOVELTY - An isolated nucleic acid molecule (I) encoding hemipteran myosin light chain kinase, is new.

DETAILED DESCRIPTION - An isolated nucleic acid molecule (I) encoding hemipteran myosin light chain kinase comprises (i) a nucleic acid sequence encoding a polypeptide comprising a sequence of 839 amino acids (SEQ ID NO: 2) or a fragment of (i) comprising at least 10 nucleotides. INDEPENDENT CLAIMS are also included for: (1) a recombinant vector comprising (I); and (2) an isolated polypeptide molecule comprising a sequence of SEQ ID NO: 2 or its fragment having at least 10 amino acids.

BIOTECHNOLOGY - Preferred Sequences: (I) comprises a sequence of 2517 bp (SEQ ID NO: 1) or its fragment having at least 10, i.e. 12-150 nucleotides. The polypeptide molecule comprises a fragment of SEQ ID NO: 2 having 12-150 amino acids.

ACTIVITY - Pesticide.

MECHANISM OF ACTION - None Given.

USE - The nucleic acid molecule and the encoded polypeptide are useful in identifying or developing compounds with activity as pesticides or as pharmaceuticals.

EXAMPLE - Test details are described but no results given. (16 pages)

L21 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:292143 HCAPLUS
DOCUMENT NUMBER: 140:317126
TITLE: Cloning and sequence of hemipteran myosin light chain kinase and potential use in development of pesticides or pharmaceuticals
INVENTOR(S): Chen, Ruihua; Chaguturu, Munirathnam K.; Yuhas, Debra; Allenza, Paul; Halling, Blaik P.
PATENT ASSIGNEE(S): FMC Corporation, USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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     WO 2004029577         A2    20040408    WO 2003-US29901        20030918
     WO 2004029577         A3    20040701
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
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     AU 2003275144         A1    20040419    AU 2003-275144         20030918
     EP 1543116            A2    20050622    EP 2003-759412         20030918
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     JP 2006500067         T     20060105    JP 2004-540171         20030918
     US 2006148031         A1    20060706    US 2005-528631         20051116
PRIORITY APPLN. INFO.:                       US 2002-413720P     P  20020926
                                             WO 2003-US29901     W  20030918
AB   The cDNA sequence and the encoded amino acid sequence of myosin
     light chain kinase from Aphis gossypii are
     disclosed.  The sequences of the invention are useful in the
     identification or development of pesticides or pharmaceuticals.


=> d his

     (FILE 'HOME' ENTERED AT 12:23:13 ON 19 JAN 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 12:23:44 ON 19 JAN 2007
L1        14613 S MYOSIN (3W) KINASE?
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L8         4169 S APHIS (W) GOSSYPII
L9            1 S L7 AND L8
L10        1431 S L7 AND MUSCLE?
L11         651 S CONTRACT? AND L10
L12         463 S PHOSPHORYLAT? AND L11
L13          47 S L12 AND (CARDIAC OR HEART)
L14          26 DUP REM L13 (21 DUPLICATES REMOVED)
                E CHEN R/AU
L15        4492 S E3
                E RUIHUA C/AU
                E HALLING B P/AU
L16          60 S E3-E6
                E YUHAS D/AU
L17          16 S E6-E9
                E ALLENZA P/AU
L18          19 S E4
                E CHAGUTURU M K/AU
L19          24 S E3-E7
L20        4599 S L15 OR L16 OR L17 OR L18 OR L19
L21           2 S L7 AND L20
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	Issue Date	Pages	Document ID	Title
1	20060706	10	US 20060148031 A1	Hemipteran myosin light chain kinase
2	20051027	75	US 20050239103 A1	Flea head, nerve cord, hindgut and malpighian tubule nucleic acid molecules, proteins and uses thereof
3	20041104	109	US 20040219525 A1	Plant polynucleotides encoding novel prenyl proteases
4	20040226	85	US 20040040054 A1	Plant polynucleotides encoding novel na+/h+ antiporters
5	20030417	74	US 20030073827 A1	Flea head, nerve cord, hindgut and malpighian tubule nucleic acid molecules, proteins and uses thereof

	Issue Date	Pages	Document ID	Title
1	20061214	78	US 20060281900 A1	Lepidoptera voltage-gated calcium channels
2	20060706	10	US 20060148031 A1	Hemipteran myosin light chain kinase
3	20051027	75	US 20050239103 A1	Flea head, nerve cord, hindgut and malpighian tubule nucleic acid molecules, proteins and uses thereof
4	20040902	54	US 20040171114 A1	Isolation and use of ryanodine receptors
5	20030417	74	US 20030073827 A1	Flea head, nerve cord, hindgut and malpighian tubule nucleic acid molecules, proteins and uses thereof
6	20020801	20	US 20020100819 A1	Multiple sprayer assembly & method for use
7	20020423	22	US 6375089 B1	Multiple sprayer assembly and method for use
8	19850716	23	US 4529813 A	Production of insecticidally active vinyl-cyclopropane carboxylic acid esters
9	19810922	23	US 4291176 A	Production of insecticidally active vinyl-cyclopropane carboxylic acid esters
10	19790102	15	US 4132784 A	(Substituted pyridyl)phenoxy phosphorus compounds and their use as insecticides

	Issue Date	Pages	Document ID	Title
11	19790102	16	US 4132783 A	(Substituted pyridyl)phenoxy phosphorus compounds and their use as insecticides

	Issue Date	Pages	Document ID	Title
1	20061221	54	US 20060288448 A1	Insect-specific protease recognition sequences
2	20061026	117	US 20060242733 A1	Bacillus Cry9 family members
3	20061026	43	US 20060241044 A1	Bacillus Cry9 family members
4	20061026	116	US 20060241043 A1	Bacillus Cry9 family members
5	20061012	107	US 20060228751 A1	Cloning and characterization of the broad-spectrum resistance gene P12
6	20060928	30	US 20060217535 A1	Hemipteran muscarinic receptor
7	20060921	59	US 20060212964 A9	Methods for enhancing insect resistance in plants
8	20060706	10	US 20060148031 A1	Hemipteran myosin light chain kinase
9	20060323	105	US 20060064775 A1	Method for increasing resistance against stress factors in plants
10	20060126	50	US 20060021096 A1	Genes encoding proteins with pesticidal activity
11	20051208	213	US 20050273881 A1	Defensin polynucleotides and methods of use
12	20051124	53	US 20050261483 A1	Genes encoding proteins with pesticidal activity
13	20051124	54	US 20050261188 A1	Genes encoding proteins with pesticidal activity
14	20050908	34	US 20050198706 A1	Lipases and methods of use

15	20050901	15	US 20050191714 A1	Proteome interaction mapping

	Issue Date	Pages	Document ID	Title
16	20050825	149	US 20050188441 A1	Lipoxygenase polynucleotides and methods of use
17	20050825	59	US 20050188439 A1	Methods for enhancing insect resistance in plants
18	20050728	28	US 20050166284 A1	Plant activation of insect toxin
19	20050721	65	US 20050158764 A1	Recombinant bHLH-PAS/JHR polypeptide and its use to screen potential insecticides
20	20050623	114	US 20050138685 A1	Bacillus Cry9 family members
21	20050616	106	US 20050132439 A1	Novel nucleic acid sequences and their use in methods for achieving pathogen resistance in plants
22	20050512	153	US 20050102717 A1	Crop plant cystatin proteinase inhibitors and methods of use
23	20050407	64	US 20050076407 A1	Plant defensin polynucleotides and methods of use thereof
24	20050331	81	US 20050070697 A1	Pathogen-responsive genes, promoters, regulatory elements, and methods of use for same
25	20050217	54	US 20050037436 A1	Test systems and the use thereof for identifying and characterizing compounds
26	20041021	51	US 20040210963 A1	Genes encoding proteins with pesticidal activity

27	20041021	107	US 2004021095 7 A1	Cloning and characterization of the broad-spectrum resistance gene P12

	Issue Date	Pages	Document ID	Title
28	20040902	54	US 20040171114 A1	Isolation and use of ryanodine receptors
29	20040729	21	US 20040148652 A1	Isolated nucleic acid molecules encoding the Dw3 P-glycoprotein of sorghum and methods of modifying growth in transgenic plants therewith
30	20040610	48	US 20040111761 A1	Sunflower anti-pathogenic proteins and genes and their uses
31	20040520	56	US 20040098769 A1	Replication protein A and use
32	20040513	56	US 20040091505 A1	Genes encoding proteins with pesticidal activity
33	20040415	47	US 20040073971 A1	Sunflower anti-pathogenic proteins and genes and their uses
34	20040408	16	US 20040068004 A1	Use of oxabicyclo[2.2.1]heptadiene derivatives as pesticidal agents
35	20040318	71	US 20040053996 A1	Use of oxabicyclo[2.2.1]heptane derivatives as pesticidal agents
36	20040311	40	US 20040049804 A1	Maize defense-inducible genes and their use
37	20031106	50	US 20030207926 A1	Isothiazole derivatives and their use as pesticides
38	20030918	117	US 20030177528 A1	Genes encoding novel proteins with pesticidal activity against Coleopterans
39	20030904	151	US 20030166855 A1	Lipoxygenase polynucleotides and methods of use

	Issue Date	Pages	Document ID	Title
40	20030828	56	US 20030163840 A1	Replication protein A and use
41	20030821	59	US 20030159185 A1	Replication protein A and use
42	20030724	45	US 20030140381 A1	Genes and regulatory DNA sequences associated with stress-related gene expression in plants and methods of using the same
43	20030724	69	US 20030140368 A1	Plant defensins
44	20030508	60	US 20030088887 A1	Compositions and methods for enhancing disease resistance in plants
45	20030227	230	US 20030041348 A1	Defensin polynucleotides and methods of use
46	20030213	29	US 20030033632 A1	Maize proteinase inhibitor-like polynucleotides and methods of use
47	20030206	35	US 20030028921 A1	Maize basal layer antimicrobial protein polynucleotides and method of use
48	20030123	73	US 20030017566 A1	Maize peroxidase genes and their use for improving plant disease resistance and stalk strength
49	20021107	24	US 20020166146 A1	Maize PR1 polynucleotides and methods of use
50	20021107	39	US 20020166143 A1	Sclerotinia-inducible genes and promoters and their uses
51	20021107	38	US 20020166141 A1	Antimicrobial peptides and methods of use

	Issue Date	Pages	Document ID	Title
52	20021031	34	US 20020162142 A1	Genes and methods for manipulation of growth
53	20021017	118	US 20020151709 A1	Genes encoding novel proteins with pesticidal activity against coleopterans
54	20021003	40	US 20020144307 A1	Plant defense-inducible genes and their use
55	20020808	59	US 20020108140 A1	COMPOSITIONS AND METHODS FOR ENHANCING DISEASE RESISTANCE IN PLANTS
56	20020627	27	US 20020083493 A1	Major latex protein gene and promoter and their uses
57	20020606	31	US 20020069428 A1	Genes encoding scip-1 orthologs and methods of use
58	20020425	28	US 20020049993 A1	Maize rhoGTPase-activating protein (rhoGAP) polynucleotides and methods of use
59	20020307	14	US 20020029392 A1	Methods for enhancing disease resistance in plants
60	20020221	39	US 20020022256 A1	Maize histone deacetylases and their use
61	20011206	34	US 20010049834 A1	Maize pathogenesis-related polynucleotide and methods of use
62	20010927	20	US 20010025380 A1	Family of maize PR-1 genes and promoters
63	20010920	22	US 20010023501 A1	Methods for making male-sterile plants
64	20010628	22	US 20010005746 A1	Stomatin-like genes and their use in plants

65	20060912	53	US 7105332 B2	Genes encoding proteins with pesticidal activity

	Issue Date	Pages	Document ID	Title
66	20060822	104	US 7094951 B2	Cloning and characterization of the broad-spectrum resistance gene Pi2
67	20060509	34	US 7041874 B2	Isolated nucleic acid molecules encoding the Br2 P-glycoprotein of maize and methods of modifying growth in plants transformed therewith
68	20051011	54	US 6953680 B2	Mitofusins, Fzo Homologs and functional derivatives thereof
69	20050726	145	US 6921847 B2	Lipoxygenase polynucleotides and methods of use
70	20050628	205	US 6911577 B2	Defensin polynucleotides and methods of use
71	20050405	88	US 6875907 B2	Antimicrobial peptides and methods of use
72	20050301	25	US 6861577 B2	Promoter of a maize major latex protein gene and methods of using it to express heterologous nucleic acids in transformed plants
73	20050215	62	US 6855865 B2	Nucleic acids encoding plant defensins and methods of use thereof
74	20040615	36	US 6750380 B1	Isolated nucleic acid moelcules encoding the Dw3 P-glycoprotein of sorghum and methods of modifying growth in transgenic plants therewith

	Issue Date	Pages	Document ID	Title
75	20040413	26	US 6720480 B2	Maize proteinase inhibitor-like polynucleotides and defense-activated promoter, transformed plants, and methods of use
76	20040323	42	US 6709865 B1	Sunflower LOX polynucleotides and related compositions
77	20040309	47	US 6703347 B2	Isothiazole derivatives and their use as pesticides
78	20031209	30	US 6660907 B2	Genes encoding SCIP-1 orthologs and methods of use
79	20031007	58	US 6630615 B1	Defense-related signaling genes and methods of use
80	20030819	58	US 6608240 B1	Sunflower disease resistance genes
81	20030701	14	US 6586657 B2	Methods for enhancing disease resistance in plants
82	20030610	40	US 6576814 B1	Manipulation of Mlo genes to enhance disease resistance in plants
83	20030325	55	US 6538176 B1	Maize replication protein A and use
84	20030225	18	US 6525175 B1	Trypsin inhibitors with insecticidal properties obtained from Pentaclethra macroloba
85	20030204	33	US 6515202 B1	Polynucleotides encoding monocot 12-oxo-phytodienoate reductases and methods of use
86	20021112	39	US 6479629 B2	Maize histone deacetylases and their use

87	20021105	14	US 6476292 B1	Methods for enhancing disease resistance in plants

	Issue Date	Pages	Document ID	Title
88	20020924	23	US 6455297 B1	Methods and compositions for regulating cell death and enhancing disease resistance to plant pathogens
89	20020827	40	US 6441275 B1	Production of pathogen resistant plants
90	20020827	29	US 6441151 B1	Plant prohibition genes and their use
91	20020813	25	US 6433249 B1	Use of .beta.-glucosidase to enhance disease resistance and resistance to insects in crop plants
92	20020806	33	US 6429362 B1	Maize PR-1 gene promoters
93	20020611	39	US 6403861 B1	Production of pathogen resistant plants
94	20020611	21	US 6403768 B1	Manipulation of Mlo genes to enhance disease resistance in plants
95	20020507	18	US 6384302 B1	Trypsin inhibitors with insecticidal properties obtained from Pentaclethra macroloba
96	20020430	39	US 6380461 B1	Production of pathogen resistant plants
97	20020430	40	US 6380460 B1	Production of pathogen resistant plants
98	20020423	39	US 6376748 B1	Production of pathogen resistant plants
99	20011204	55	US 6326165 B1	Recombinant BHLH-PAS/JHR polypeptide and its use to screen potential insecticides

	Issue Date	Pages	Document ID	Title
100	20010911	41	US 6287843 B1	Maize histone deacetylases and their use
101	20010807	24	US 6271439 B1	Methods and compositions for regulating cell death and enhancing disease resistance to plant pathogens
102	20010403	22	US 6211433 B1	Manipulation of Mlo genes to enhance disease resistance in plants
103	20010306	21	US 6198020 B1	Nitric oxide as an activator of the plant pathogen defense systems
104	20001226	39	US 6166291 A	Production of pathogen resistant plants
105	20000222	49	US 6027876 A	Method for monitoring pesticide resistance
106	19991214	125	US 6001981 A	Synthetic modification of Spinosyn compounds
107	19991123	23	US 5990140 A	Substituted oxazolines of the formula (I)
108	19991109	21	US 5981722 A	Trypsin inhibitors with insecticidal properties obtained from pentaclethra macroloba
109	19981124	43	US 5840861 A	A83543 compounds and process for production thereof
110	19980616	26	US 5767253 A	A83543 Compounds; factors Q, R, S, and T
111	19970923	41	US 5670364 A	A83543 compounds and process for production thereof
112	19970520	26	US 5631155 A	Saccharopolyspora spinosa strain

	Issue Date	Pages	Document ID	Title
113	19970107	26	US 5591606 A	Process for the production of A83543 compounds with Saccharopolyspora spinosa
114	19961105	42	US 5571901 A	Insecticide and miticide compositions containing A83543 compounds
115	19960305	41	US 5496931 A	Insecticide and miticide A83543 compounds and their method of production by fermentation
116	19940315	29	US 5294622 A	Substituted quinolines and cinnolines